



RPP:156A-US

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Yasmin Thanavala et al. Art Unit: 1651  
Serial No: 09/420,695  
Filed: 10/19/1999  
Examiner: M. Flood  
For: ORAL IMMUNOLOGY  
USING PLANT PRODUCT  
CONTAINING HEPATITIS  
SURFACE ANTIGEN

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Dr. Yasmin Thanavala declares:

1. That she is a named inventor in the above identified patent application;
2. That in 1969 she graduated from the University of Bombay, India with a Bachelor of Science Degree in microbiology and a minor in chemistry;
3. That in 1973 she graduated from the University of Bombay with a Masters Degree in immunology;
4. That in 1979 she graduated from the University of London with a Ph.D. in immunology;

5. That from 1979 to 1985 she worked as a Research Associate at the Middlesex Hospital Medical School, London, England on a project for the World Health Organization;

6. That in 1985 she was a Research Affiliate in the Department of Immunology at Roswell Park Cancer Institute, Buffalo, New York;

7. That from 1985 to 1999 she was a Cancer Research Scientist II-IV, Department of Molecular Immunology, Roswell Park Cancer Institute, Buffalo, New York;

8. That since 1986 she has been a Research Professor at Niagara University, Niagara Falls, New York;

9. That since 1997 she has been a Professor in the Department of Microbiology/Immunology at the State University of New York at Buffalo, Roswell Park Division;

10. That since 1999 she has been a Member of the Department of Immunology, Roswell Park Cancer Institute, Buffalo, New York;

11. That under her direction and supervision, transgenic tomatoes expressing hepatitis B surface antigen (HBsAg) were tested for ability to raise an immune response as follows:

a) Lyophilized tomatoes expressing HBsAg prepared essentially as described in U.S. Patent 5,914,123 were obtained;

b) The lyophilized tomatoes plus cholera toxin (CT) mucosal adjuvant were fed to Balb/C mice once a week for three consecutive weeks. Each mouse was given one gram of the lyophilized tomatoes containing about 66.6  $\mu$ g HBsAg per gram of

lyophilized tomatoes. 10 $\mu$ g of CT adjuvant was added into a volume of 100 $\mu$ l phosphate buffered saline (PBS) and the mixture added to the tomatoes just prior to feeding. No discernable primary HBsAg-specific antibody response was elicited in the mice as a result of the above attempted immunization;

12. That under her direction and supervision, transgenic tomatoes expressing hepatitis B surface antigen (HBsAg) were further tested for ability to raise an immune response as follows:

a) Lyophilized tomatoes expressing HBsAg prepared essentially as described in U.S. Patent 5,914,123 were obtained;

b) Balb/C mice were primed subcutaneously with a single sub-immunogenic dose of yeast derived recombinant HBsAg.

c) The lyophilized tomatoes were fed to treated Balb/C mice. Each mouse was given one gram of the lyophilized tomatoes containing about 66.6  $\mu$ g HBsAg per gram of lyophilized tomatoes on days 56, 63 and 70 with CT adjuvant as above described;

13. That the above examples indicate that oral immunization does not occur simply by the feeding of tomatoes expressing HBsAg as incorrectly suggested in U.S. Patent 5,914,123 and that further U.S. Patent 5,914,123 does not teach or suggest how an oral immunization might be obtained by the feeding of tomatoes expressing HBsAg whether or not U.S. Patent 5,914,123 is considered with Kaprowski et al and Stites et al. cited by the Examiner in the above identified patent application;

14. That further, neither the above results nor the teachings of the above cited references teach or suggest how an oral immunization against HBsAg or any other non-enteric pathogen might be obtained by the feeding of plant material expressing an antigen for the pathogen;

15. That she further declares that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: January 4<sup>th</sup>, 2001

Yasmin Thanavala  
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